Prospective Validation of the Prognostic Usefulness of Brain Natriuretic Peptide in Asymptomatic Patients With Chronic Severe Mitral Regurgitation

Rodolfo Pizarro, MD, Oscar O. Bazzino, MD, Pablo F. Oberti, MD, Mariano Falconi, MD, Federico Achilli, MD, Anibal Arias, MD, Juan G. Krauss, MD, Arturo M. Cagide, MD

Buenos Aires, Argentina

Objectives

The purpose of the study was to determine the independent and additive prognostic value of brain natriuretic peptide (BNP) in patients with severe asymptomatic mitral regurgitation and normal left ventricular function.

Background

Early surgery could be advisable in selected patients with chronic severe mitral regurgitation, but there are no criteria to identify candidates who could benefit from this strategy. Assessment of BNP has not been studied in asymptomatic patients with severe mitral regurgitation; hence, its prognostic value remains unclear.

Methods

We prospectively evaluated 269 consecutive patients with severe asymptomatic organic mitral regurgitation and left ventricular ejection fraction above 60%. The first 167 consecutive patients served as the derivation cohort, and the following 102 patients served as a validation cohort. The combined end point was the occurrence of either symptoms of congestive heart failure, left ventricular dysfunction, or death at follow-up.

Results

The end point was reached in 35 (21%) patients of the derivation set and in 21 (20.6%) patients of the validation cohort. The receiver-operating characteristics curve yielded an optimal cutoff point of 105 pg/ml of BNP that was able to discriminate patients at higher risk in both cohorts (76% vs. 5.4% and 66% vs. 4.0%, respectively). In both sets, BNP was the strongest independent predictor by multivariate analysis.

Conclusions

Among patients with severe asymptomatic organic mitral regurgitation, BNP ≥105 pg/ml discriminates a subgroup of patients at higher risk. Because of its incremental prognostic value, BNP assessment should be considered in clinical routine workup for risk stratification. (J Am Coll Cardiol 2009;54:1099–106) © 2009 by the American College of Cardiology Foundation

Severe organic mitral regurgitation is a progressive disease with a high incidence of events in the long-term follow-up (1–4). Usually, surgical treatment is recommended based on the presence of symptoms of congestive heart failure (CHF), the appearance of left ventricular dysfunction, and less frequently, because of the amount of regurgitation (1,2,5). In contrast, the indication of early surgical treatment in patients suitable for this intervention, but who do not have symptoms of heart failure or left ventricular dysfunction, is controversial. In this particular subset of patients, there are no strong indicators useful for the recommendation of early surgical intervention.

For this purpose, the prognostic value of several echocardiographic parameters has been assessed in different studies. Specifically, end-systolic diameter and left atrial size, as well as both ejection fraction and ventricular size, have been found to allow risk stratification in asymptomatic patients (5–7). Another marker of hemodynamic consequences, the effective regurgitant orifice area (EROA), has also been shown to correlate with an adverse outcome (7,8).

In recent years (9–11), the measurement of natriuretic peptides in patients with heart failure has become important. The brain natriuretic peptide (BNP) and its inactive amino-terminal portion (NT-proBNP), both result from the breakdown of proBNP. These hormones have vasodilator and diuretic effects, are antagonists of the adrenergic and renin-angiotensin systems, and are released in response...
2. Preserved exercise tolerance defined by an exercise electrocardiogram with Bruce protocol and the following requirements: functional capacity ≥7 metabolic equivalents of task (METs) without symptoms or any of the following: complex ventricular arrhythmia, hypotension, or pathological ST-T segment deviation (8).

We excluded patients with associated valve disease (aortic valve disease, moderate or severe mitral stenosis, or significant right organic valve disease), ischemic mitral regurgitation, previous valve or coronary surgery, cardiomyopathies or pericardial diseases, patients with terminal disease whose expected survival was <1 year, patients with poor echocardiographic acoustic window, and those who did not complete the initial exercise test requirements.

Follow-up was complete in all but 6 cases (4 patients of the derivation set and 2 patients of the validation set).

Clinical data. At entry, complete clinical evaluation was performed in all patients. Decisions about valve surgery were left to the treating physicians, who were unaware of the BNP results.

Echocardiographic data. All studies were performed with Hewlett Packard Sonos 5500 equipment (Andover, Massachusetts). Studies included a spectral, continuous, and color Doppler transthoracic echocardiographic examination in all patients. The degree of mitral regurgitation was quantified in relation to the classical color Doppler parameters (12).

Left ventricular volumes and left ventricular ejection fraction were measured by Simpson's biplane technique (13). End-diastolic and -systolic diameters were indexed by body surface area (BSA) (end-diastolic diameter/BSA and end-systolic diameter/BSA) (14). Atrial volume (AV) was indexed by BSA (AV/BSA), and pulmonary artery systolic pressures were measured classically. The presence of a new flail leaflet (NFL) was also assessed (14–16).

We measured regurgitant volume, regurgitant fraction, and EROA (as an average of the quantitative method, and the proximal isovelocity area method, PISA) (17,18).

The echocardiographic readings were carried out by 2 independent observers, who were blinded to the clinical and biochemistry information.

Biochemistry data. Blood samples were obtained in all patients 24 h after enrollment in the echocardiography laboratory and repeated 1 year later. Venous blood samples were obtained on usual medications with the patient resting quietly while semirecumbent. The samples were placed immediately on ice, and plasma was stored at −80°C before being assayed for BNP using standard radioimmunoassay (19).

End point definition. The combined end point consisted of the appearance of either CHF or left ventricular dysfunction, or the occurrence of death (LVDSD) during follow-up. The presence of CHF was defined as the onset of dyspnea in New York Heart Association (NYHA) functional class III to IV, requiring sustained pharmacologic treatment or hospitalization.

New onset of left ventricular dysfunction was defined as the assessment of an ejection fraction below 60% (7,9) during follow-up.

All outcomes were assessed by 2 investigators blinded to the echocardiographic clinical data. Patients referred for surgery without symptoms or low ejection fraction (decisions regarding surgery left to treating physician) were counted as not reaching an end point in the analysis.
Follow-up. Clinical and echocardiographic evaluations were performed at least yearly during a follow-up visit. Patients who died or underwent surgery were censored the same day, and those who remained alive were censored at the end of follow-up.

Statistical analysis. All results for continuous variables are expressed as mean ± SD, and skewed variables are expressed as median and interquartile range (IQR). For groupwise comparisons of continuous variables, the Mann-Whitney U and Student t tests were used for skewed and normally distributed variables, respectively. For categorical variables, the Fisher exact test or the chi-square test were used. The cutoff level for each echocardiographic variable was obtained from previous studies (8). The cutoff level for METs, AV/BSA, and ejection fraction were set according to the receiver-operating characteristic (ROC) curve analysis.

The cutoff level for BNP was set according to the ROC curve analysis. The BNP value showing the maximum likelihood ratio in the curve was established as the cutoff point between low and high BNP. This cutoff point was prospectively tested in the validation set.

Survival analysis was assessed using the Kaplan-Meier method. Nonadjusted comparison of time to the event was based on the log-rank test.

Logistic regression models were developed to analyze the effect of clinical and echocardiographic variables on the observed association between basal BNP levels and the risk of the combined end point. For the assessment of linearity, we grouped BNP concentrations and the echocardiographic variables into quartiles. Then we fitted a logistic regression model for the prediction of the combined end point, with the lowest quartile serving as the reference group, and plotted the average value of each quartile versus the coefficient of the quartile. The plot was then examined with respect to the shape of the resulting curve. Variables showing lack of linearity were logarithmically transformed.

The multivariate logistic regression models incorporated clinical and echocardiographic variables that proved to be related to the combined end point on univariate analysis.

To assess the statistical significance of BNP values, we adjusted the p values using the Bonferroni correction, dividing the usual statistically significant p value (0.05) by the number of variables in the model.

To facilitate the clinical interpretation, we repeated the multivariate analysis entering BNP and the echocardiographic measurements as dichotomous variables with the cutoff points that were previously described.

Calibration and discrimination of the logistic models were tested with the Hosmer-Lemeshow test and comparison of the ROC curves of the derivation and validation sets.

Comparison between ROC curves was performed with the ROC analyser program version 6.0.

The statistical analysis was performed with STATA version 8.0 software (College Station, Texas). A p value <0.05 was considered significant, and all tests performed were 2-tailed.

Results

Baseline characteristics. A total of 269 patients were included, 167 in the derivation cohort and 102 in the validation cohort. Median BNP values (IQR 25% to 75%) at entry were similar in both sets, 21 (IQR 9 to 247) and 27 (IQR 7 to 241) in the derivation and validation cohorts, respectively. The areas of the ROC curves relating baseline BNP levels to the combined end point were 0.80 ± 0.05 and 0.81 ± 0.04 in the

| Table 1 Basal Characteristics in Relation to BNP Levels |
|-----------------|-----------------|-----------------|-----------------|
|                 | Derivation Set   | Validation Set  |
|                 | BNP <105 pg/ml   | BNP ≥105 pg/ml  | BNP <105 pg/ml  | BNP ≥105 pg/ml  |
|                 | (n = 130)        | (n = 37)        | (n = 75)        | (n = 27)        |
| Age (yrs)       | 61 ± 6          | 66 ± 8          | 62 ± 5          | 65 ± 7          |
| Male            | 77 (59)         | 24 (64)         | 47 (63)         | 18 (65)         |
| Atrial fibrillation | 12 (9)       | 5 (13)          | 5 (6.6)         | 3 (7.4)         |
| Hypertension    | 20 (15)         | 8 (21)          | 9 (12)          | 3 (10)          |
| Systolic arterial pressure (mm Hg) | 139 ± 22 (93-170) | 135 ± 18 (90-155) | 137 ± 28 (91-160) | 136 ± 21 (90-150) |
| Heart rate (beats/min) | 76 ± 10 (62-98) | 69 ± 11 (55-89) | 75 ± 10 (60-101) | 70 ± 12 (65-94) |
| NFL, n (%)      | 2 (1.5)         | 1 (10)          | 1 (1.3)         | 1 (3.7)         |
| Exercise capacity (METs) | 9.5 (8.5-11) | 9.0 (8.0-12) | 9.0 (8.0-14) | 8.5 (7.5-11) |
| Ejection fraction (%) | 68 (65-72) | 65 (63-68) | 68 (65-70) | 66 (63-69) |
| End-diastolic diameter/BSA (mm/m²) | 33 (25-38) | 40 (29-46) | 32 (24-37) | 39 (31-45) |
| Regurgitant volume (ml/beat) | 65 (63-70) | 76 (66-84) | 66 (62-71) | 76 (68-86) |
| Regurgitant fraction (%) | 50 (46-55) | 58 (49-64) | 49 (45-57) | 60 (52-67) |
| AV/BSA (cm²/m²) | 52 (46-61) | 65 (47-74) | 46 (44-57) | 67 (49-81) |
| Pulmonary artery systolic pressure (mm Hg) | 24 (18-30) | 32 (24-38) | 25 (15-29) | 35 (22-39) |

Values are expressed as mean ± SD, n (%), or median (interquartile range). AV = atrial volume; BNP = brain natriuretic protein; BSA = body surface area; EROA = effective regurgitant orifice area; METs = metabolic equivalents of task; NFL = new flail leaflet.
Mitral valve surgery was performed in 30 patients (29%) of the validation set. Nineteen patients (63%) underwent mitral valve repair and 11 patients (37%) mitral valve replacement. Eleven patients did not reach the combined end point but underwent surgery, as indicated by their referring physician. These patients were not significantly different with regard to clinical and echocardiographic variables from patients who reached the combined end point, and the median BNP value of these 11 patients was 39 (IQR 21 to 93).

**Predictive value of BNP. Univariate analysis.** When we stratified BNP according to quartiles: ≤20, 21 to 69, 70 to 104, and ≥105 pg/ml, patients’ event-free survival at 48 months was as follows: 99 ± 4%, 97 ± 7%, 93 ± 6%, and 29 ± 8%, respectively. BNP values were higher in patients reaching LVDSD in both the derivation (median 117, IQR 87 to 194 vs. median 38, IQR 19 to 67, p < 0.0001) and also in the validation sets (median 114, IQR 79 to 187 vs. median 35, IQR 20 to 64).

The rate of the combined end point was higher in patients with BNP ≥105 pg/ml than in patients with BNP <105 pg/ml in the derivation set (76% vs. 5.4%; p < 0.00001, Fisher exact test) and also in the validation set (66% vs. 4%; p < 0.00001, Fisher exact test) (Fig. 1).

In the Kaplan-Meier analysis, BNP values were dichotomized at this cutoff point, and they were able to discriminate patients with a higher risk of LVDSD in the derivation set (log-rank: 16.2, adjusted hazard ratio [HR]: 5.6; 95% CI: 2.9 to 10.6, p < 0.00001) and also in the validation set (log-rank: 13.2, adjusted HR: 4.7; 95% CI: 2.4 to 11.3, p < 0.00001) (Figs. 2A and 2B).

Applying this cutoff value, sensitivity, specificity, negative predictive value, and positive predictive value to predict LVDSD in the derivation set were 80%, 93%, 94%, and

![](https://example.com/image.png)

**Figure 1 Combined End Point According to BNP Values**

Symptoms of congestive heart failure, left ventricular systolic dysfunction, or death (LVDSD) according to brain natriuretic peptide (BNP) values.
76%, respectively, whereas in the validation set, values were 85%, 89%, 96%, and 66%, respectively.

Table 2 shows the relationship between baseline variables and prognosis. In both sets, univariate markers of worse evolution were BNP, end-systolic diameter/BSA, end-diastolic diameter/BSA, EROA, regurgitant volume AV/BSA, age, pulmonary artery systolic pressures, atrial fibrillation, ejection fraction, and NFL.

**MULTIVARIATE ANALYSIS.** In the derivation set, all variables significantly associated with the end point were included in a logistic regression analysis. In our first model, we used log transformation of the continuous variables. In the derivation cohort, the independent predictors were: BNP (odds ratio [OR]: 3.89; 95% CI: 2.52 to 17.57, \( p < 0.0001 \)), end-systolic diameter/BSA (OR: 3.14; 95% CI: 1.82 to 15.92, \( p < 0.01 \)), and EROA (OR: 3.57; 95% CI: 2.27 to 16.45, \( p < 0.001 \)).

When we entered all markers in the logistic model as categorical variables, BNP \( \geq 105 \) pg/ml was the strongest independent predictor of LVDSD with an OR: 4.6; 95% CI: 2.7 to 11.6, \( p < 0.0001 \). Other independent prognostic variables were: end-systolic diameter/BSA \( \geq 22 \) mm/m\(^2\) (OR: 3.4; 95% CI: 1.6 to 10.7, \( p < 0.01 \)), and EROA \( > 55 \) mm\(^2\) (OR: 4.2, 95% CI: 2.1 to 11.4, \( p < 0.001 \)) (Table 3).

In the validation set, multivariate analysis determined that the following variables were independent predictors: BNP \( \geq 105 \) pg/ml (OR: 4.1; 95% CI: 2.7 to 12.6, \( p = 0.0001 \)), EROA \( > 55 \) mm\(^2\) (OR: 3.7, 95% CI: 2.4 to 11.9, \( p = 0.001 \)), and end-systolic diameter/BSA \( > 22 \) mm/m\(^2\) (HR: 3.1, 95% CI: 1.8 to 13.7, \( p < 0.02 \)); Hosmer-Lemeshow test, \( p = 0.147 \) (Table 3).

The addition of BNP to the non-BNP model (EROA, end-systolic diameter/BSA, and AV) significantly increased the area under the ROC curve from 0.80 to 0.91 (\( p < 0.01 \)).

### Table 2 Univariate Predictors of LVDSD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Derivation Set (n = 167)</th>
<th>Validation Set (n = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>Age &gt;70 yrs</td>
<td>1.9 (1.4–7.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Exercise capacity &lt;9 METs</td>
<td>1.09 (0.78–7.85)</td>
<td>0.19</td>
</tr>
<tr>
<td>Ejection fraction &lt;68%</td>
<td>2.0 (1.27–11.8)</td>
<td>0.036</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.2 (1.4–8.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>NFL</td>
<td>2.3 (1.5–13.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>BNP ( \geq 105 ) pg/ml</td>
<td>4.8 (2.5–11.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>End-diastolic diameter/BSA ( &gt;35 ) mm/m(^2)</td>
<td>2.2 (1.7–14.3)</td>
<td>0.01</td>
</tr>
<tr>
<td>End-systolic diameter/BSA ( &gt;22 ) mm/m(^2)</td>
<td>3.6 (2.1–10.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Regurgitant volume &gt;65 ml/beat</td>
<td>2.7 (1.3–10.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>EROA ( &gt;55 ) mm(^2)</td>
<td>4.4 (2.2–10.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>AV/BSA ( &gt;70 ) cm(^2)/m(^2)</td>
<td>2.4 (1.7–11.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure ( &gt;35 ) mm Hg</td>
<td>1.92 (1.47–9.47)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; CI = confidence interval; LVDSD = left ventricular dysfunction, symptoms of congestive heart failure, or death; OR = odds ratio; other abbreviations as in Table 1.
in the derivation set and from 0.79 to 0.89 (p = 0.01) in the validation set (Fig. 3).

**Serial BNP measurements.** Patients who reached an end point had a higher rate of increase in BNP levels at 1 year than patients with an uneventful course (rate of increase of 26 ± 11 pg/ml vs. 9 ± 4 pg/ml, p = 0.0001, in the derivation set, and 23 ± 10 pg/ml vs. 8 ± 4 pg/ml, p = 0.001, in the validation set).

Among patients with baseline BNP values below 105 pg/ml, 5 (3%) exhibited a BNP elevation above that level at 1 year in the derivation set, and 4 patients (5.3%) did so in the validation set. All of these patients had LVSD at follow-up.

By Kaplan-Meier analysis, patients with an increased BNP over 105 pg/ml at 1 year had a worse outcome than patients who persisted with BNP < 105 pg/ml (log-rank test: 19.2, adjusted HR: 9.6; 95% CI: 4.9 to 26.6, p < 0.0001). Similar findings were observed in the validation set (log-rank test: 17.8, adjusted HR: 9.6; 95% CI: 3.9 to 21.3, p < 0.0001).

**Discussion**

The main conclusion of this study is that in asymptomatic patients with severe organic mitral regurgitation and no impairment in left ventricular function, BNP level at baseline has independent prognostic importance.

Our study also confirms that in this type of patient, echocardiographic parameters such as end-systolic diameter and EROA are also independent predictors of adverse outcome. However, according to our results, BNP is an even

| Table 3 Multivariate Analysis to Predict the Combined End Point (Derivation Set) |
|---------------------------------|-----------------|-----------------|
| OR (95% CI) p Value             |
| BNP ≥ 105 pg/ml                 | 4.6 (2.7–11.6)  | 0.0001          |
| End-systolic diameter/BSA > 22 mm² | 3.4 (1.6–10.7) | 0.01            |
| EROA > 55 mm²                   | 4.2 (2.1–11.4)  | 0.001           |

BNP = brain natriuretic peptide; other abbreviations as in Tables 1 and 2.
stronger prognostic marker than end-systolic diameter or EROA and contributes independent prognostic information additional to that provided by these echocardiographic parameters. As shown, after the addition of BNP to the echocardiographic model, the area under the ROC curve increased significantly both in the derivation and the validation set.

Furthermore, we determined and validated an optimal cutoff point for BNP of 105 pg/ml, thereby identifying asymptomatic patients with severe mitral regurgitation and preserved left ventricular systolic function who are at higher risk. In our study, BNP \( \geq 105 \text{ pg/ml} \) predicted the appearance of LVDSD with additional information barely affected by the adjustments for end-systolic diameter and EROA.

Another point to consider is the value of the repeated measurements of BNP. Patients with a greater BNP increase at 1 year had a worse subsequent course.

Why are these findings of clinical importance? As admitted by current guidelines, patients with severe mitral regurgitation complicated with heart failure or left ventricular systolic dysfunction carry a severe prognosis and should be promptly referred for surgical treatment. Conversely, early surgery is controversial in asymptomatic patients with normal left ventricular function because this group is considered to be at low risk. However, our findings indicate that this group includes patients with a heterogeneous prognosis, some of whom are at higher risk and cannot be identified using current risk stratification schemes. Moreover, other studies by our group performed in a similar population have also shown that these patients are at high risk for an adverse outcome, as evidenced by a rate of LVDSD of 6.7%/year (7). This high rate of progression in a short-term follow-up emphasizes the need for improvement of the current risk stratification schemes.

Because there is a paucity of clinical predictors for the prognostic assessment of these patients, risk stratification relies almost exclusively on echocardiographic measurements. Our data led us to conclude that the addition of BNP measurements to the echocardiographic predictors could improve risk stratification and facilitate the early and timely indication of valve surgery.

This is an important clinical objective. In this subset of asymptomatic patients, nonrandomized studies demonstrated that the strategy of early surgery was associated with an improvement in the long-term event rate by decreasing cardiac mortality and the incidence of episodes of congestive heart failure requiring hospitalization (20,21). Early surgery can avoid the appearance of major complications, but can also improve post-operative results. It has been reported that once symptoms or left ventricular dysfunction develop, post-operative outcome becomes worse at medium- and long-term follow-up (22).

Which are the mechanisms responsible for the prognostic significance of elevated BNP in this particular group of patients? As determined in previous studies (7,8), end-systolic diameter and the EROA entail prognostic value, probably because they reflect ventricular overload and the consequences of valve disease progression (7,8). In our study, these parameters also showed independent prognostic value, but the prognostic value of BNP was independent and additional to these parameters. This finding suggests that BNP is not merely a surrogate of the consequences of mitral regurgitation.

Other investigations concluded that natriuretic peptides poorly correlate with diastolic and systolic diameters (\( r = 0.26 \) and \( r = 0.16 \), respectively), EROA (\( r = 0.17 \)), and the left atrial volume (\( r = 0.5 \)) (23,24).

Several efforts have been made to identify a parameter able to demonstrate ventricular dysfunction, which is not so evident by classical noninvasive methods (23,25). In experimental models, the transition from compensated to decompensated ventricular function increases the synthesis and secretion of BNP (26). Experimental and clinical data reinforce the hypothesis that higher BNP levels in patients with preserved left ventricular function at rest could represent subclinical ventricular dysfunction (26,27). Thus, these data led us to speculate that the elevations of this peptide in asymptomatic patients may indicate the presence of subtle myocardial impairment elicited by longstanding volume overload.

Few studies have evaluated the relation between BNP and clinical events in organic mitral regurgitation, and to date, there is a lack of information regarding its usefulness in asymptomatic patients (24,28).

Sutton et al. (29) concluded that natriuretic peptides could be useful to determine prognosis in asymptomatic patients with severe mitral regurgitation. Also, this study demonstrated that natriuretic peptide levels were higher in asymptomatic patients than in normal controls (29).

Detaint et al. (24) concluded that elevated BNP levels are independently associated with higher mortality rates and the combined end point of death or heart failure. A cutoff value of BNP >31 pg/ml was also established that identified patients with lower survival rates and higher rates of death and CHF.

There are important differences between our investigation and that of Detaint et al. (24). First, all patients in our study were asymptomatic, whereas in their study a significant number of patients with clinical symptoms of heart failure were included. Second, we established a cutoff value of BNP by prospective validation in a separate cohort. Most important, in our study group, mitral regurgitation was severe in only 35% of patients, whereas in our study group, all patients had severe mitral regurgitation.

**Study limitations.** This study shows the association of BNP with the combined end point of heart failure, left ventricular systolic dysfunction, or death. We focused on the major consequences of severe mitral regurgitation, but a cost/benefit analysis of the BNP-based strategy and also further outcome analysis should be performed.

Among the confounders of the association of interest, we have not included the end-systolic and -diastolic ventricular volumes because they are part of the ejection fraction formula.
We believe that the lack of tissue Doppler measurements is another limitation of this study. Additionally, exercise stress echocardiography was not performed in our study, and recent studies comparing the results of such tests to progression of BNP levels indicate its prognostic value (30,31).

Finally, we should mention that the model could be overfitted when applied to the validation set.

Conclusions

In asymptomatic patients with severe mitral regurgitation and preserved left ventricular function, risk stratification for identification of surgical candidates is controversial. In this context, the identification of a reliable prognostic marker is of clinical relevance to facilitate the identification of patients who could benefit from early and timely surgery.

Because of its independent and incremental prognostic value, BNP assessment should be considered in the clinical routine workup to risk stratify this group of patients.

Reprint requests and correspondence: Dr. Mariano Falconi, Cardiology Division, Hospital Italiano de Buenos Aires, Gascon 450, Ciudad Autonoma de Buenos Aires, Buenos Aires 1181, Argentina. E-mail: mariano.falconi@hospitalitaliano.org.ar.

REFERENCES


Key Words: mitral regurgitation • natriuretic peptide • prognosis.